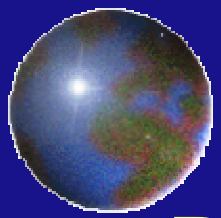
Laboratory Diagnostics



Bonna Cunningham, MS

North Dakota Public Health Laboratory

SARS Testing* at CDC

- Antibody Tests
- Molecular Test
- Cell Culture

* *SARS serologic and molecular assays will be available at the NDPHL shortly (pending release by CDC).*

Antibody Tests

- IFA and ELISA
  - Reliable 21 days post onset of fever
  - Antibodies detected as early as 14 days in some cases

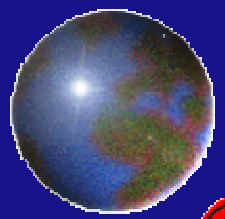
Molecular Test

- RT-PCR
  - Positives reported
  - Negatives repeated with more sensitive primers when available

Viral Culture

- Respiratory secretions and blood
  - Vero, Vero E6 support virus replication
  - Other cell lines being evaluated

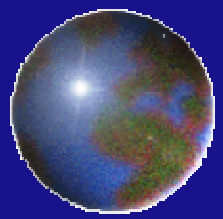
Interpreting Test Results



- **Positive**
  - Indicates current or recent infection with the coronavirus.
- **Negative**
  - Does not mean the patient does not have SARS.
  - Diagnose on clinical evaluation and possible past exposure.

Potential SARS Specimens

- Serum
  - 5-10 ml blood in serum separator
- EDTA whole blood
  - 5-10 ml
- Stool
  - 10-50 cc
- NP swabs/OP swabs
  - Dacron swab in viral transport

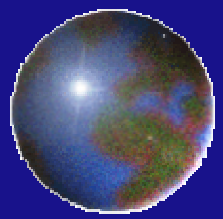


M4 Viral Transports

Insert illustration

Location of M4 Viral Transports in North Dakota

- Two M4 viral transports/swabs in each smallpox shipper
  - Four shippers at each NDLRN Level A laboratory
  - Four shippers at each District Health Unit
- Additional six M4 viral transports/swabs at each District Health Unit



Level A Labs

Insert MAP

District Public Health Units

Insert MAP

Packaging and Shipping

- **Follow IATA/DOT packaging regulations for Diagnostic Specimens***

- http://www.cdc.gov/ncidod/sars/packingspecimens-sars.htm

**** "Smallpox shippers" issued by NDDoH meet requirements***

Smallpox Shippers

(Insert Illustration)

- Contact the NDPHL for assistance
  - Phone Number: 701.328.5262

Laboratory Biosafety

- Establish protocols to protect laboratory workers
  - Labeling suspected SARS cases
  - Handling blood specimens for routine testing
  - Handling specimens for microbiological analysis
  - Define BSL-2 practices*
  - Define BSL-3 practices*

*Refer to CDC/NIH Biosafety in Microbiological and Biomedical Laboratories manual (BMBL):

http://www.cdc.gov/od/ohs/biosfty/bmb14/bmb143s3.ht

Blood Specimens for Routine Testing

- Use universal precautions
- Wear appropriate PPE
  - Disposable gloves
  - Lab coat
  - Eye/face shields
- Use safe centrifugation practices

Centrifuging Protocols

- Use sealed centrifuge cups or rotors
  - Load and unload in BSC
- If sealed centrifuge cups and BSC not available
  - Keep testing to a minimum
  - Centrifuge separately
  - Limit number of staff in room where centrifuge is located
  - Use respiratory protection when unloading centrifuge
    - N-95 mask
    - Eye/face shields

BSL-2 Activities

- Exam/processing of formalin-fixed tissues
- Molecular analysis of extracted preps
- EM with glutaraldehyde-fixed grids
- Routine exam of bacterial/mycotic cultures
- Routine staining/analysis of fixed smears
- Packaging specimens for transport

--Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS, Department of Health and Human Services, Centers for Disease Control and Prevention, April 2, 2003

BSL-2 Activities/BSL-3 Practices

- Aliquoting/diluting specimens
- Inoculating bacterial/mycotic culture media
- Microbiology testing other than propagation of viral agents
- Nucleic acid extractions of untreated specimens
- Prep/fixing of smears for micro analysis

--Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS, Department of Health and Human Services, Centers for Disease Control and Prevention, April 2, 2003

BSL-3 Activities

- Viral cell culture
- Initial characterization of viral agents in cultures of SARS specimens

--Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with SARS, Department of Health and Human Services, Centers for Disease Control and Prevention, April 2, 2003

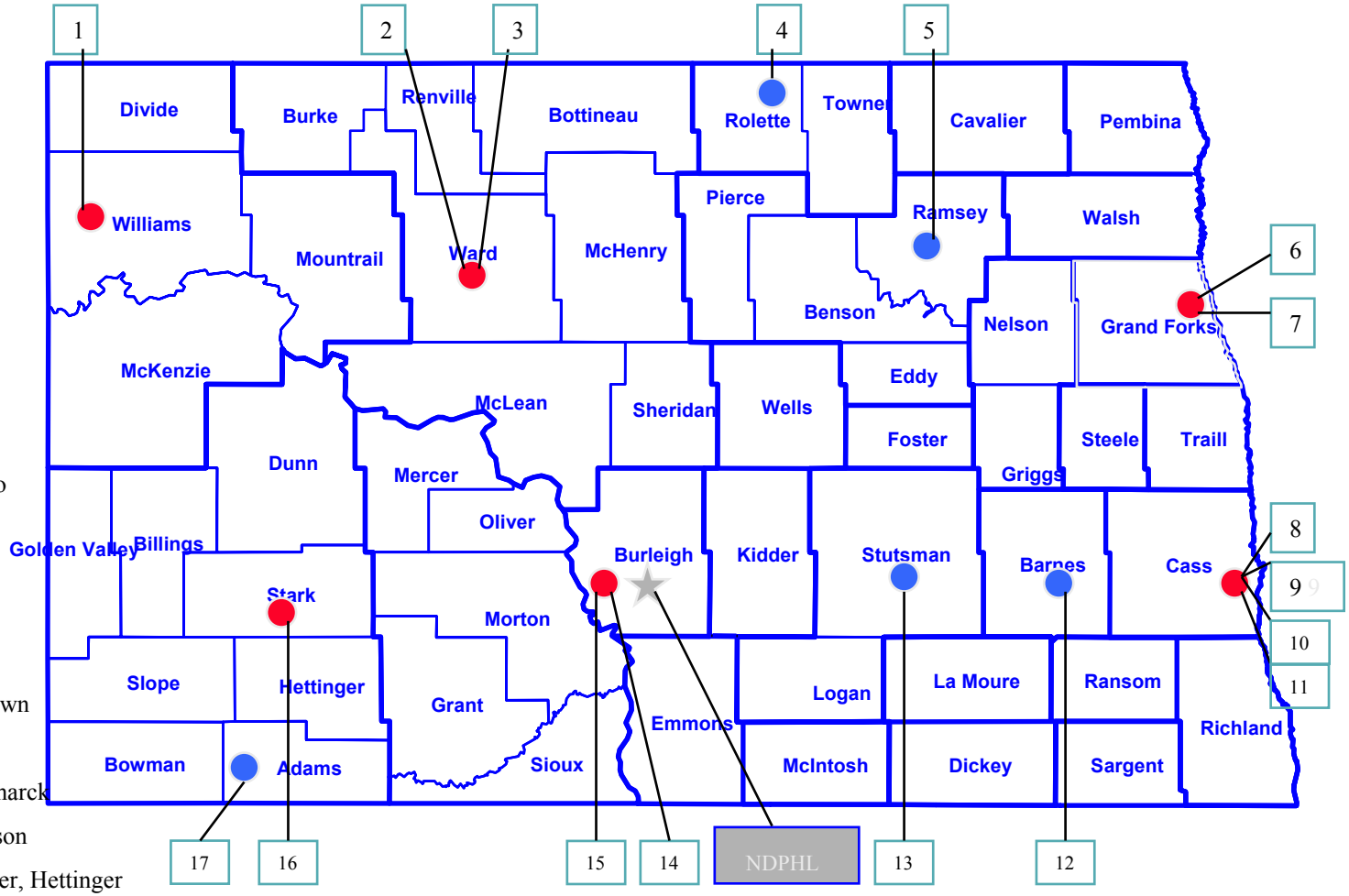
NDDoH Website

http://www.health.state.nd.us/disease/SARS

North Dakota Laboratory Response Network

Level-A Laboratories

1. Mercy Hospital, Williston
2. Trinity Med. Cen., Minot
3. USAFB, Minot
4. Presentation Hospital, Rolla
5. Mercy Hosp, Devils Lake
6. USAFB, Grand Forks
7. Altru Hospital, Grand Forks
8. Innovis Health Center, Fargo
9. MeritCare Med Cen., Fargo
10. VA Medical Center, Fargo
11. Dakota Clinic, Fargo
12. Mercy Hosp., Valley City
13. Health Care Hosp., Jamestown
14. MedCenter One, Bismarck
15. St. Alexius Med. Cen., Bismarck
16. St. Joseph Hospital, Dickinson
17. West River Reg. Med. Center, Hettinger



Level-B/C Laboratory

North Dakota Public Health Laboratory (NDPHL)

Severe Acute Respiratory Syndrome (SARS)

Larry A. Shireley, MS, MPH
State Epidemiologist
North Dakota Department of Health

CDC SARS Case Definition April 10, 2003

- Onset since February 1, 2003
- Measured temperature ≥ 100.5^0F
- Respiratory Illness*

AND

- Travel within 10 days of symptoms onset to:
  - Peoples' Republic of China, Hong Kong, Hanoi, Viet Nam or Singapore

OR

- Close contact within 10 days of symptoms onset to:
  - Suspected SARS case
  - Respiratory illness & travel to above areas

* WHO definition requires radiographic evidence of infiltrates consistent with pneumonia or respiratory distress syndrome

Epidemiology

- Transmission
  - Person – Person
  - Health Care Workers
  - Community Transmission
- United States –
  - Primarily related to travel
- Primarily adults – 25 – 70
  - Uncommon < 15 years old

Epidemiology

- Most Cases Resolve
  - ~90%+ day 6-7
  - Mortality ~ 4 %
- United States
  - Cases less severe
  - Reasons?
    - Cultural?
    - Medical care?
    - Other co-infection?

SARS Time Line

- November 16, 2002
  - Index Case – Guangdong, China
  - (Reported Feb 14, 2003)
- Feb 11, 2003 - First Case Reports from China
- Feb 21 Hong Kong hotel outbreak
- Feb 28, 2003 – Viet Nam reports cases
- Global Alert – March 12, 2003
- March 14 – Canada reports cases
- March 15 – WHO Travel Advisory
- March 24 – Link to coronavirus
- April 3 – CDC Travel Advisory
- April 4 – Executive Order - Quarantine

Cumulative number of reported suspect and probable cases (SARS)

1 November 2002 - 3 April 2003 , 17:00 GMT+2

Disclaimer: The presentation of material on the maps contained herein does not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or areas or its authorities of its frontiers or boundaries.

LEGEND

Cumulative number of case(s)

- 1 - 9
- 10 - 99
- 100 - 499
- 500 - 999
- 1000 - 1499

Number of deaths

- 1 - 9
- 10 - 19
- 20 - 29
- 30 - 39
- 40 - 49

§ Due to differences in the case definitions being used at a national level, probable cases are reported by all countries except the United States of America, which is reporting suspect cases under investigation.

* One death attributed to Hong Kong Special Administrative Region of China occurred in a case medically transferred from Viet Nam.

Suspected Cases Worldwide (April 12, 2003)

- **Total Cases** 2,960
  - **Deaths** 119
- **Number of Countries** 19

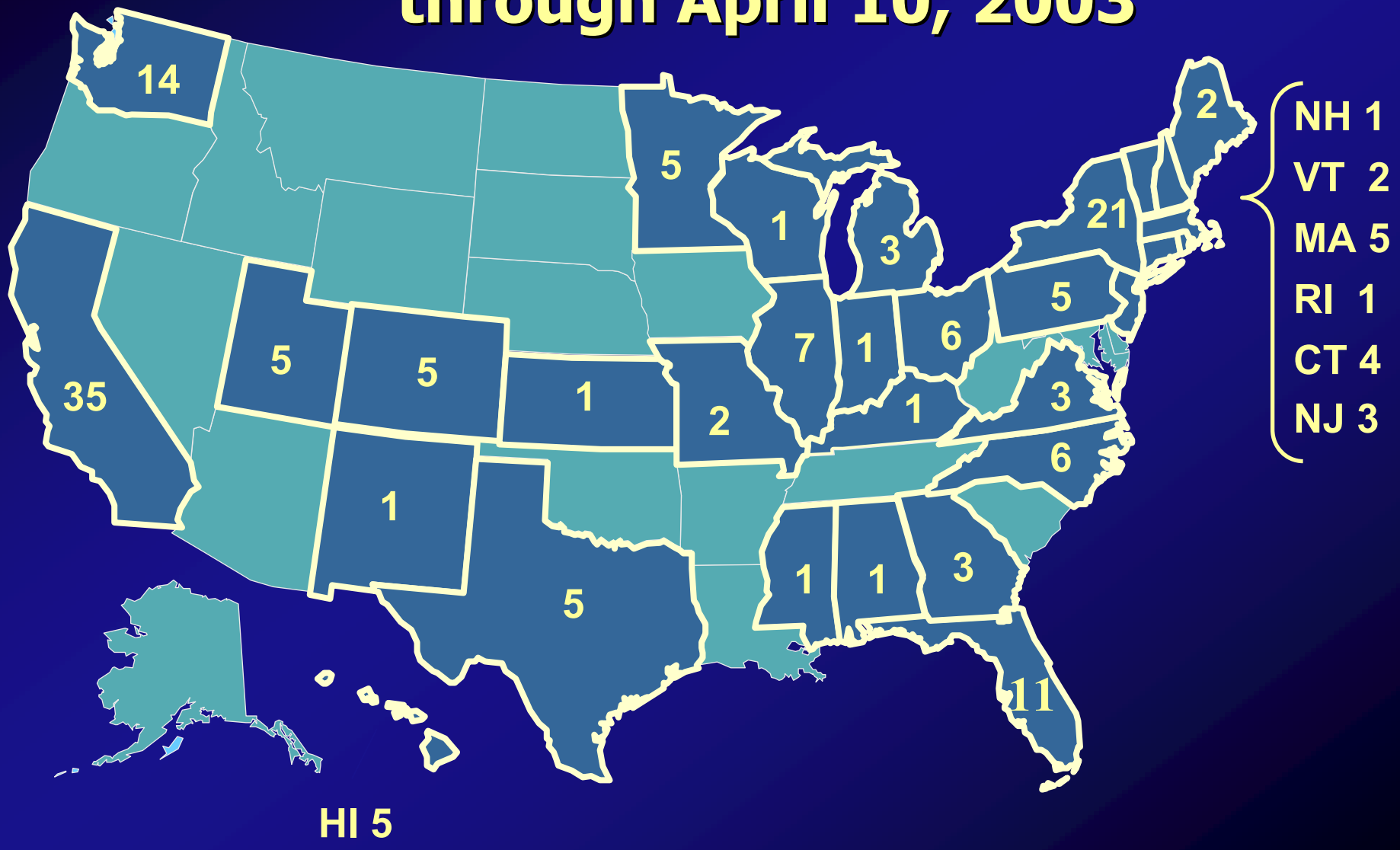
Suspected SARS Cases by Country April 12, 2003

Country	Cases	New Cases	Deaths	Recovered	Local Transmission
Brazil	2	0	0	0	No
Canada	101	3	10	26	Yes
China	1,309	19	58	1,037	Yes
Hong Kong	1,108	49	35	215	Yes
Taiwan	23	2	0	7	Yes
France	5	0	0	1	No
Germany	6	0	0	4	No
Ireland	1	0	0	1	No
Italy	3	0	0	2	No
Japan	4	0	0	0	No
Kuwait	1	0	0	0	No

Suspected SARS Cases by Country April 12, 2003 (cont)

Country	Cases	New Cases	Deaths	Recovered	Local Transmission
Malaysia	4	0	1	0	No
Romania	1	0	0	NA	No
Singapore	147	14	9	77	Yes
South Africa	1	0	0	0	No
Spain	1	0	0	0	No
Switzerland	1	0	0	1	No
Thailand	8	1	2	5	No
United Kingdom	6	1	0	3	Yes
United States	166	0	0	NA	Yes
Viet Nam	62	1	4	46	Yes
Total	2,960	90	119	1,425	

Reported Suspect Cases of SARS
United States
through April 10, 2003

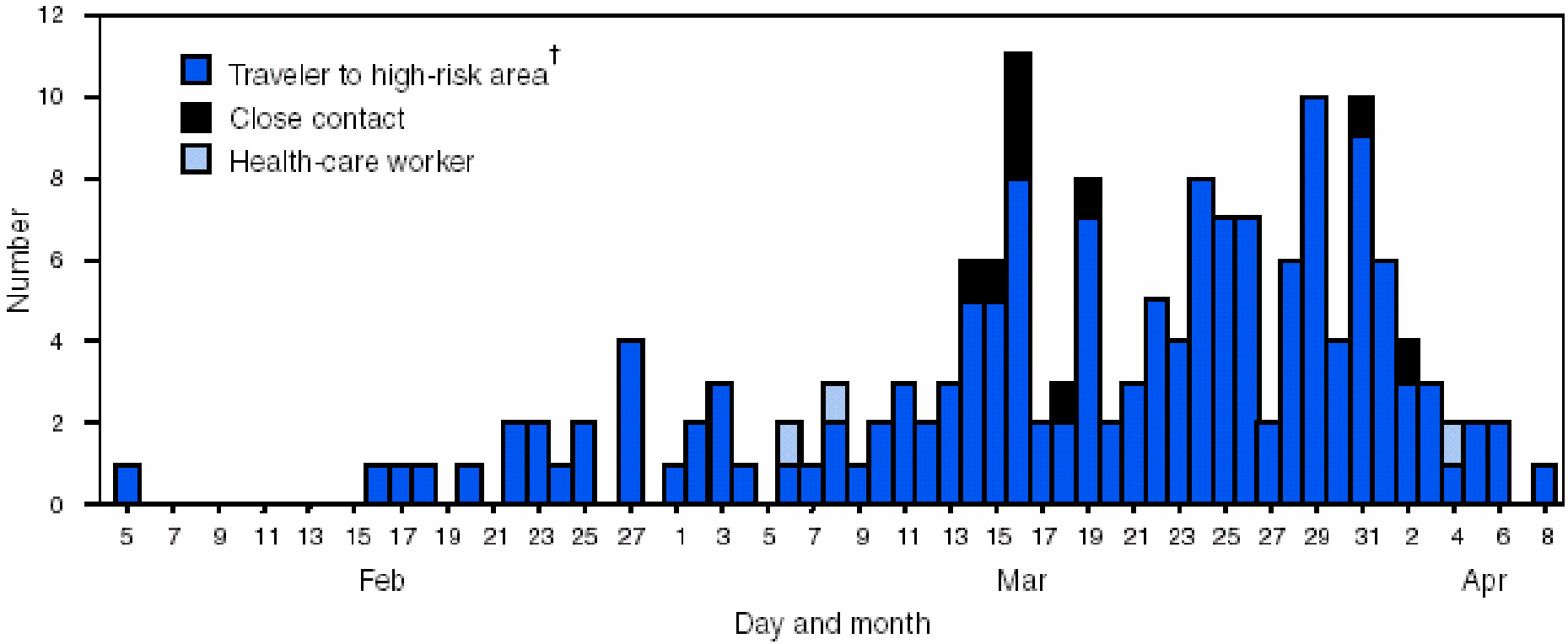


Characteristics of US SARS Cases* As of April 9, 2003

- 135 (81%) Adults
- 154 (93%) Travel to endemic area
- 9 (5%) Household contact to SARS
- 3 (2%) Health Care Workers
- 60 (36%) Hospitalized >24 hours
- 33 (20%) Radiographic abnormalities

*166 cases

Number of Suspected Cases of SARS by Exposure Category and Date of Illness Onset United States, 2002



* N = 166.
† Mainland China, Hong Kong, Singapore, or Hanoi.

Number and Percentage of Reported SARS Cases by Selected Characteristics

United States, 2003

Characteristic	No.	(%)
Age (yrs)		
0–4	15	(9)
5–17	10	(6)
18–64	114	(69)
≥65	21	(13)
Unknown	6	(3)
Sex		
Female	85	(51)
Male	79	(48)
Unknown	2	(1)
Race		
White	96	(58)
Black	3	(2)
Asian	53	(32)
Unknown	14	(8)
Exposure		
Travel†	154	(93)
Close contact	9	(5)
Health-care worker	3	(2)
Hospitalized >24 hours§		
Yes	60	(36)
No	102	(62)
Unknown	4	(2)
Chest radiograph findings		
Pneumonia or RDS¶	33	(20)
Within normal limits	87	(52)
No or unknown results	46	(28)
Required mechanical ventilation		
Yes	1	(<1)
No	149	(90)
Unknown	16	(10)

* N = 166.

†To mainland China, Hong Kong, Hanoi, or Singapore.

§ As of April 9, no deaths of SARS patients have been reported in the United States.

¶ Respiratory distress syndrome.

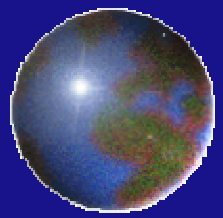
CDC, MMWR April 11, 2003

Keys to Control

- Early recognition and treatment of cases
- Stringent Infection Control Procedures in Hospitals and Clinics
- Prompt Reporting of Suspected Cases
- Investigation & Contact Tracing
- Public Awareness and Education

“We've never faced anything on this scale with such a global reach.”

-Dr. David Heymann, World Health Organization



SARS

Severe Acute Respiratory Syndrome

Clinical Issues

SARS Background

- 26 Feb 03 1st case Hanoi
  - WHO official - Dr. Carlo Urbani
    - died 29 Mar 03 SARS

SARS Background

Case 1

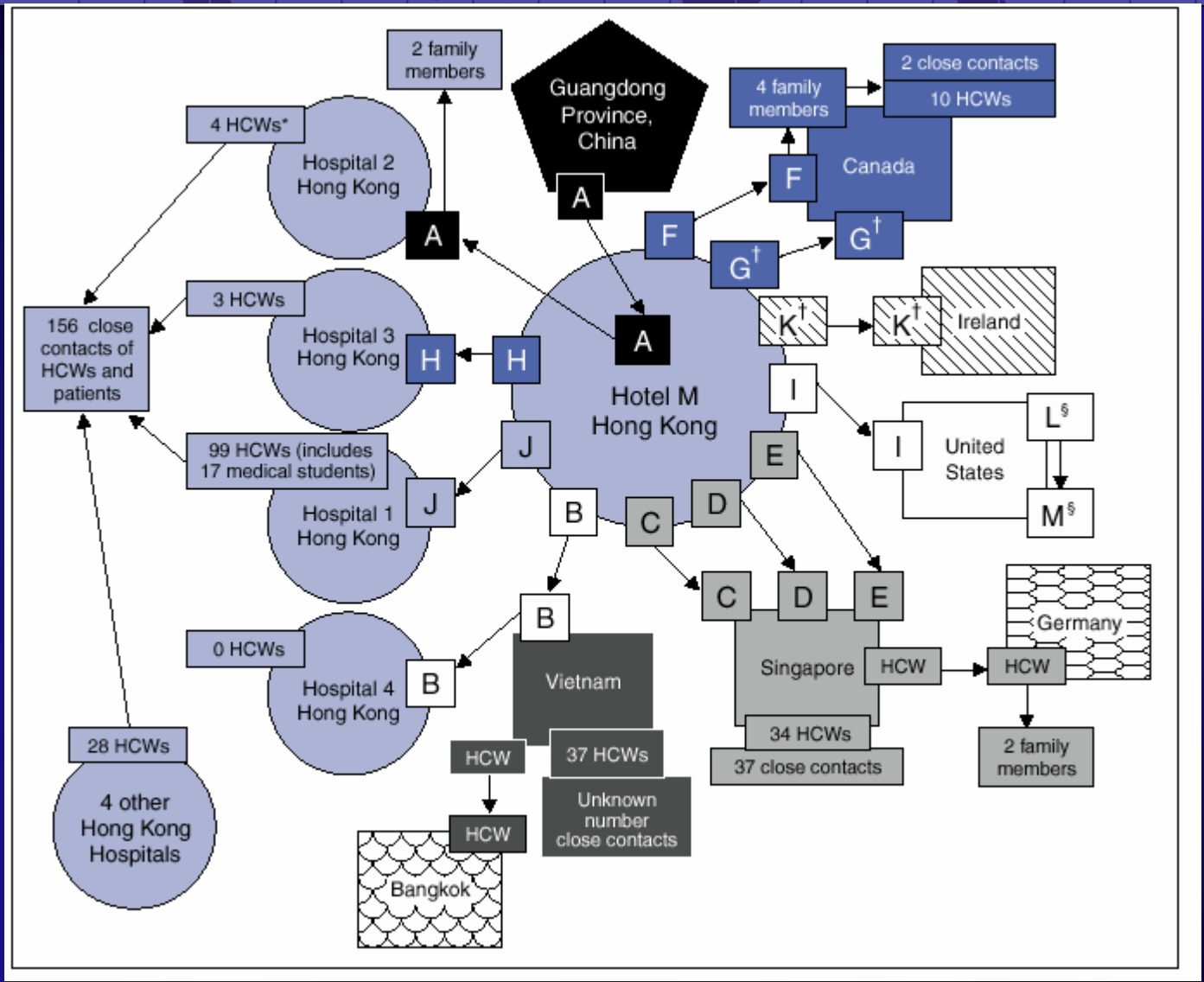
- Disease symptom onset Feb. 15
- Traveled from Guangdong Province to Hong Kong Hotel M Feb 21
- Died Feb 23
- 4 health care workers and 2 family contacts, and 10 hotel guests developed disease

SARS Background

Case 2

- Admitted to a Hanoi hospital Feb 26
- Travel to Hong Kong Hotel M
- Respiratory failure requiring ventilatory support
- Evacuated to Hong Kong; died March 12
- 59 contacts developed disease

Chain of Transmission at Hotel M - Hong Kong 2003



MMWR March 28, 2003 / 52(12);241-248

TABLE. Number* and percentage of reported severe acute respiratory syndrome cases, by selected characteristics — United States, 2003

Characteristic	No.	(%)
Age (yrs)		
0–4	9	(9)
5–17	5	(5)
18–64	71	(71)
≥65	10	(10)
Unknown	5	(5)
Sex		
Female	48	(48)
Male	49	(49)
Unknown	3	(3)
Race		
White	50	(50)
Black	1	(1)
Asian	37	(37)
Unknown	12	(12)
Exposure		
Travel†	94	(94)
Close contact	4	(4)
Health-care worker	2	(2)
Hospitalized >24 hours		
Yes	40	(40)
No	58	(58)
Unknown	2	(2)
Chest radiograph findings		
Pneumonia or RDS§	23	(23)
Within normal limits	53	(53)
No or unknown results	24	(24)
Required mechanical ventilation		
Yes	1	(1)
No	93	(93)
Unknown	6	(6)

* n = 100.
† To mainland China, Hong Kong, Hanoi, or Singapore.
§ Respiratory distress syndrome.

MMWR April 4, 2003 / 52(13);269-272

TABLE. Exposure category, clinical features, and demographics of reported severe acute respiratory syndrome (SARS) cases* — selected locations, 2003

Category	Hong Kong No.	Hong Kong (%)	Vietnam No.	Vietnam (%)	Thailand No.	Thailand (%)	Taiwan No.	Taiwan (%)	United States No.	United States (%)
Total cases†	**290§** (As of 3/25/03–S/P)	**(100)**	**59** (As of 3/24/03–P)	**(100)**	**4** (As of 3/23/03–S/P)	**(100)**	**6** (As of 3/25/03–P)	**(100)**	**51§** (As of 3/26/03–S)	**(100)**
Exposure										
Health-care worker	134	(46)	37	(63)	1	(25)	0		2	(4)
Close contact¶	156	**	NA††		0		2	(33)	5	(10)
Clinical features										
Ever hospitalized	290	(100)§	59	(100)	4	(100)	6	(100)	20§	(39)
Pneumonia	286	(99)	NA		3	(75)	6	(100)	14	(27)
Ever ventilated	NA		5	(9)	1	(25)	2	(33)	1	(2)
Dead	10	(4)§	2	(3)	0		0		0§	
Demographics										
Age	NA		Median: 38 yrs (range: 18–66 yrs)		Median: 38 yrs (range: 1–49 yrs)		Median: 53 yrs (range: 25–64 yrs)		Median: 42 yrs (range: 8 mos–78 yrs)	
Sex§§	NA									
Female	Approximately 50%		37	(63)	1	(25)	3	(50)	26	(51)
Male	Approximately 50%		22	(37)	3	(75)	3	(50)	25	(49)

* Locations used different SARS case definitions.
† S = Suspected case; P = Probable case; U = Unknown.
§ One U.S. resident (Patient B) was hospitalized in Vietnam and died in Hong Kong before he could return to the United States. He is counted as a Hong Kong case.
¶ Person having cared for, lived with, or had direct contact with respiratory secretions and body fluids of a person with SARS.
** Of the 290 SARS patients in Hong Kong, most of the remaining 156 patients are believed to be close contacts.
†† Not Available.
§§ Only percentages were reported for sex data.

MMWR March 28, 2003 / 52(12);241-248

Hong Kong

study of 50 cases

www.thelancet.com 8 Apr 03

Clinical symptoms*	Number (%)
Fever	50 (100)
Chill or rigors	37 (74)
Cough	31 (62)
Myalgia	27 (54)
Malaise	25 (50)
Running nose	12 (24)
Sore throat	10 (20)
Shortness of breath	10 (20)
Anorexia	10 (20)
Diarrhoea	5 (10)
Headache	10 (20)
Dizziness	6 (12)

*Truncal maculopapular rash was noted in one patient.

Table 1: **Symptoms of 50 patients with SARS at presentation**

Laboratory variables	Mean (range)	Number (%) of abnormal	Normal range
Haemoglobin	12·9 (8·9–15·9)	..	11·5–16·5 g/dL
Anaemia	..	9 (18%)	..
White-cell count	5·17 (1·1–11·4)	..	4–11×10⁹/L
Leucopenia	..	13 (26%)	..
Lymphocyte count	0·78 (0·3–1·5)	..	1·5–4·0×10⁹/L
Severe lymphopenia (<1·0×10⁹ /L)	..	34 (68%)	..
Platelet count	174 (88–351)	..	150–400×10⁹/L
Thrombocytopenia	..	20 (40%)	..
Alanine aminotransferase	63 (11–350)	..	6–53 U/L
Raised alanine aminotransferase	..	17 (34%)	..
Albumin	37 (26–50)	..	42–54 g/L
Low albumin	..	34 (68%)	..
Globulin	33 (21–42)	..	24–36 g/L
Raised globulin	..	10 (20%)	..
Creatinine kinase	244 (31–1379)	..	34–138 U/L
Raised creatinine kinase	..	13 (26%)	..

Table 2: **Initial laboratory findings of 50 patients with SARS**

Predictors of "severe" SARS in Hong Kong

www.thelancet.com 8 Apr 03

	Complicated (n=19)	Uncomplicated (n=31)	p
age	49.5	39	0.005
comorbidity	5	1	0.05

DM

HTN

Chronic active hepatitis

Cardiomopathy

Predictors of "severe" SARS

www.thelancet.com 8 Apr 03

- Method of contact
  - Travel to china
  - HCW
  - Hospital visit
  - Household contact ← P = 0.09
  - Social contact

Predictors of "severe" SARS

www.thelancet.com 8 Apr 03

- Duration of symptoms before admission ~ 5 days
- Temperature on admission 38.8
- WBC
- Initial lymphocyte 0.66 vs .85 ← P=0.04
- Thrombocytopenia
- Impaired LFT's 11 vs. 6 ← P = 0.01

Predictors of "severe" SARS

www.thelancet.com 8 Apr 03

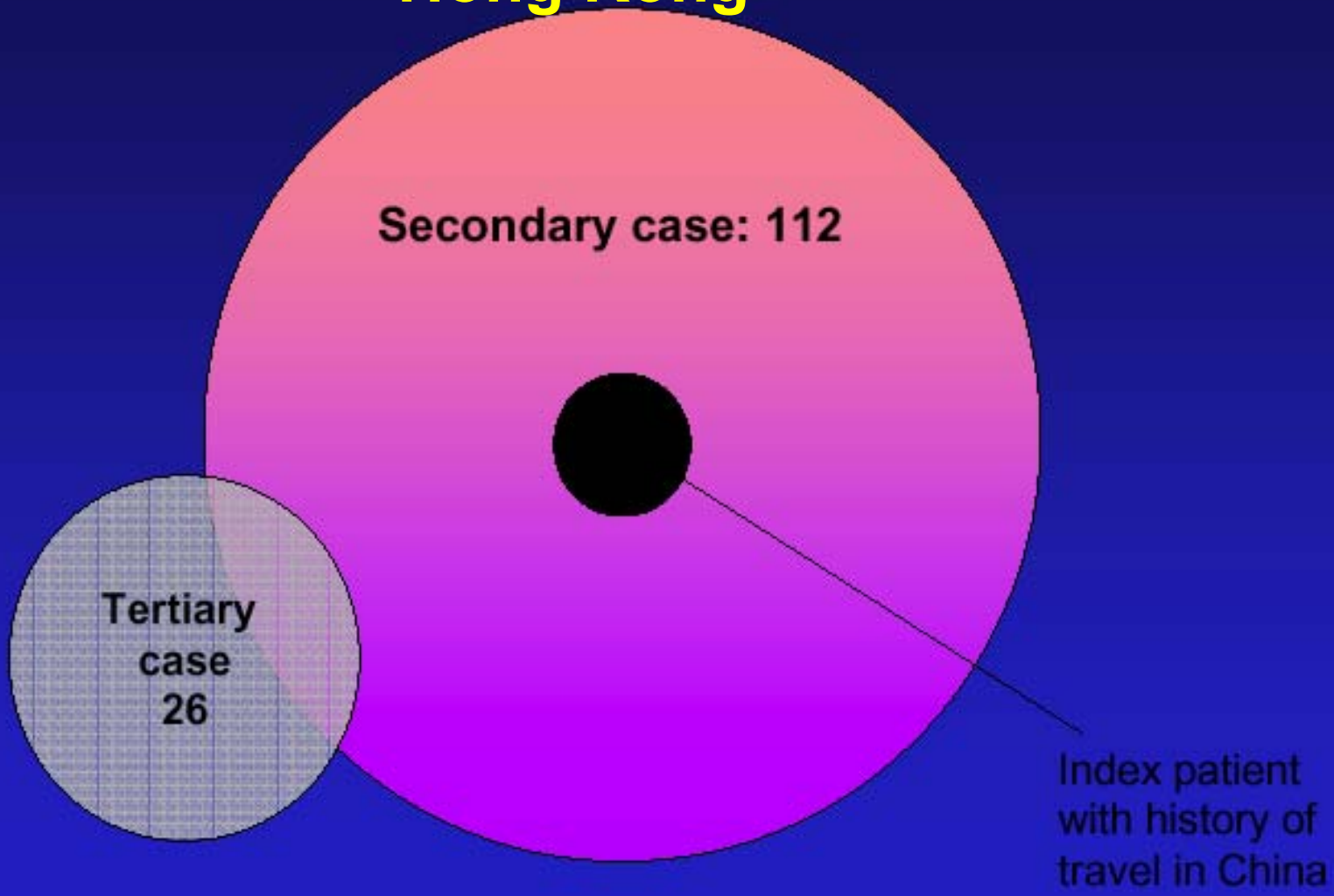
	Complicated	Uncomplicated	p
# pt on ribivirin and steroids (R&S)	18	31	
Mean days to start R&S	7.7	5.7	0.03
Start R&S after worsening	12	0	0.0001
Response to R&S	11	28	0.02

Outbreak
Hong Kong

- March 10, 18 HCW reported sick
- March 11, 50 HCW screened, 23 admitted to hospital
- March 25, 156 admitted (including 138 with direct/indirect contact with index case)

Outbreak

Hong Kong

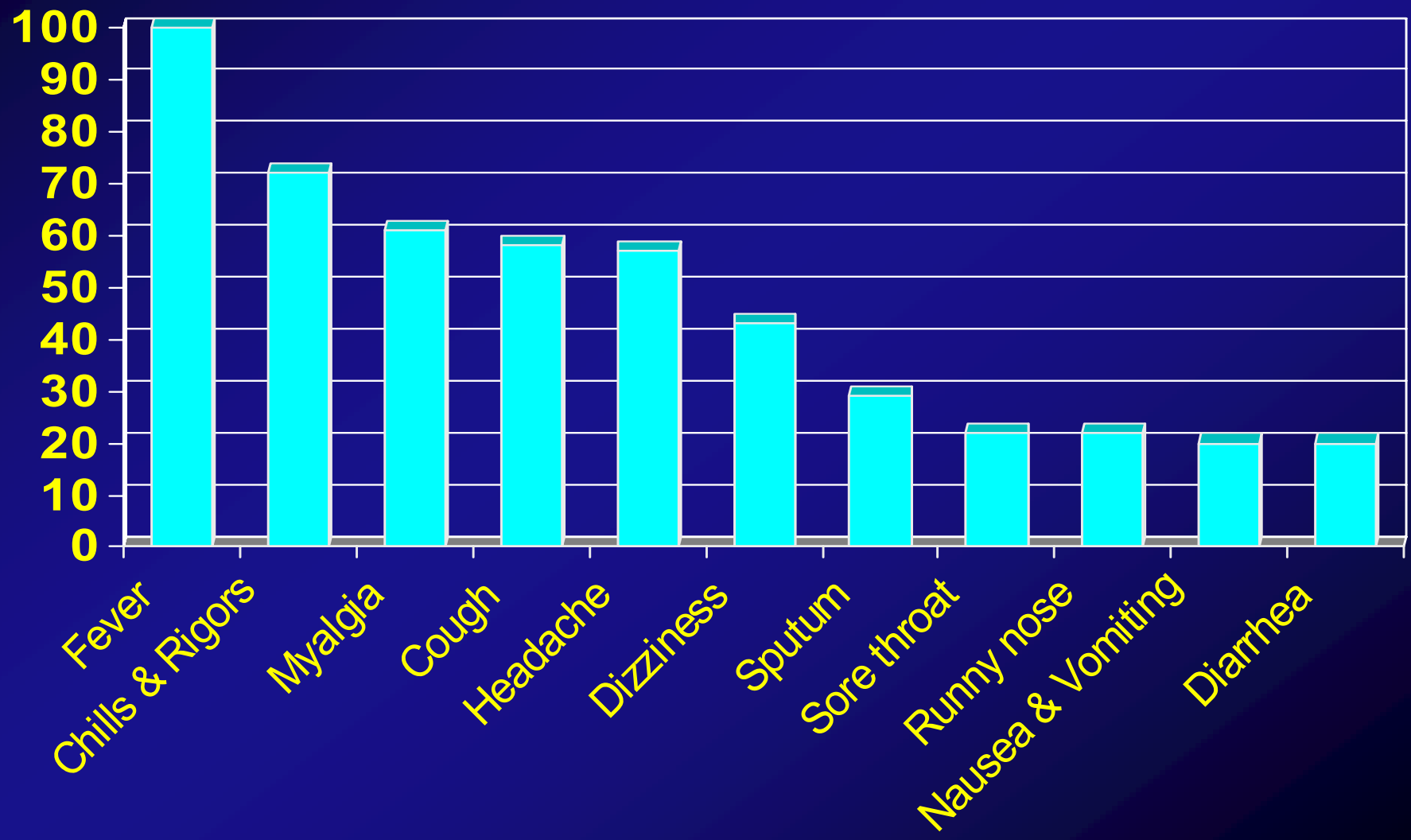


Demography
Hong Kong

- Total 138
- Female 72
- HCW 69
  - Doctors 20
  - Nurses 34
  - Allied health workers 15
- Medical Students 16
- Patients 19
- Relatives 34

Common Symptoms

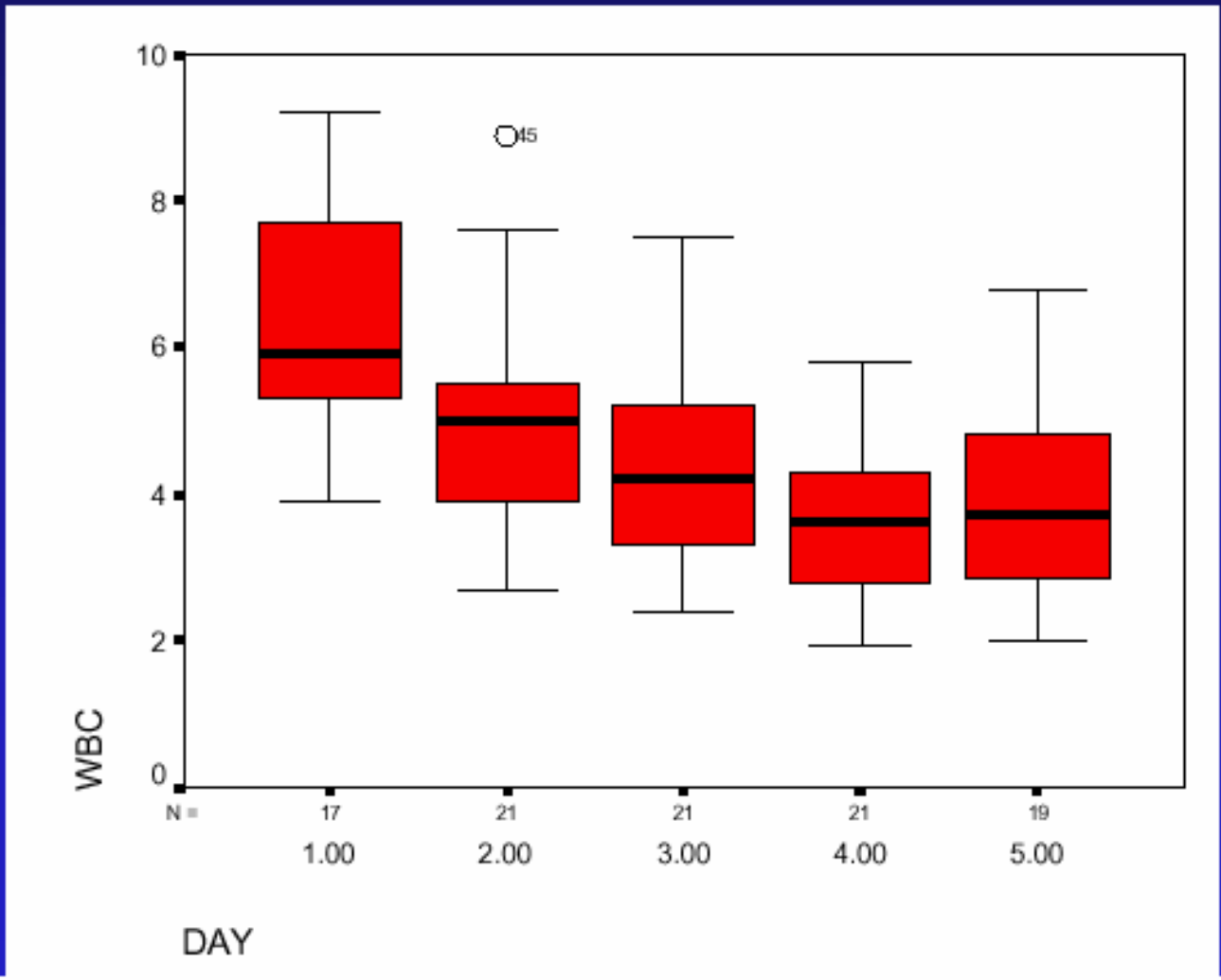
Hong Kong



Leucopenia

Hong Kong

Leucopenia (WBC<3.5x10^9/L): 33.9%



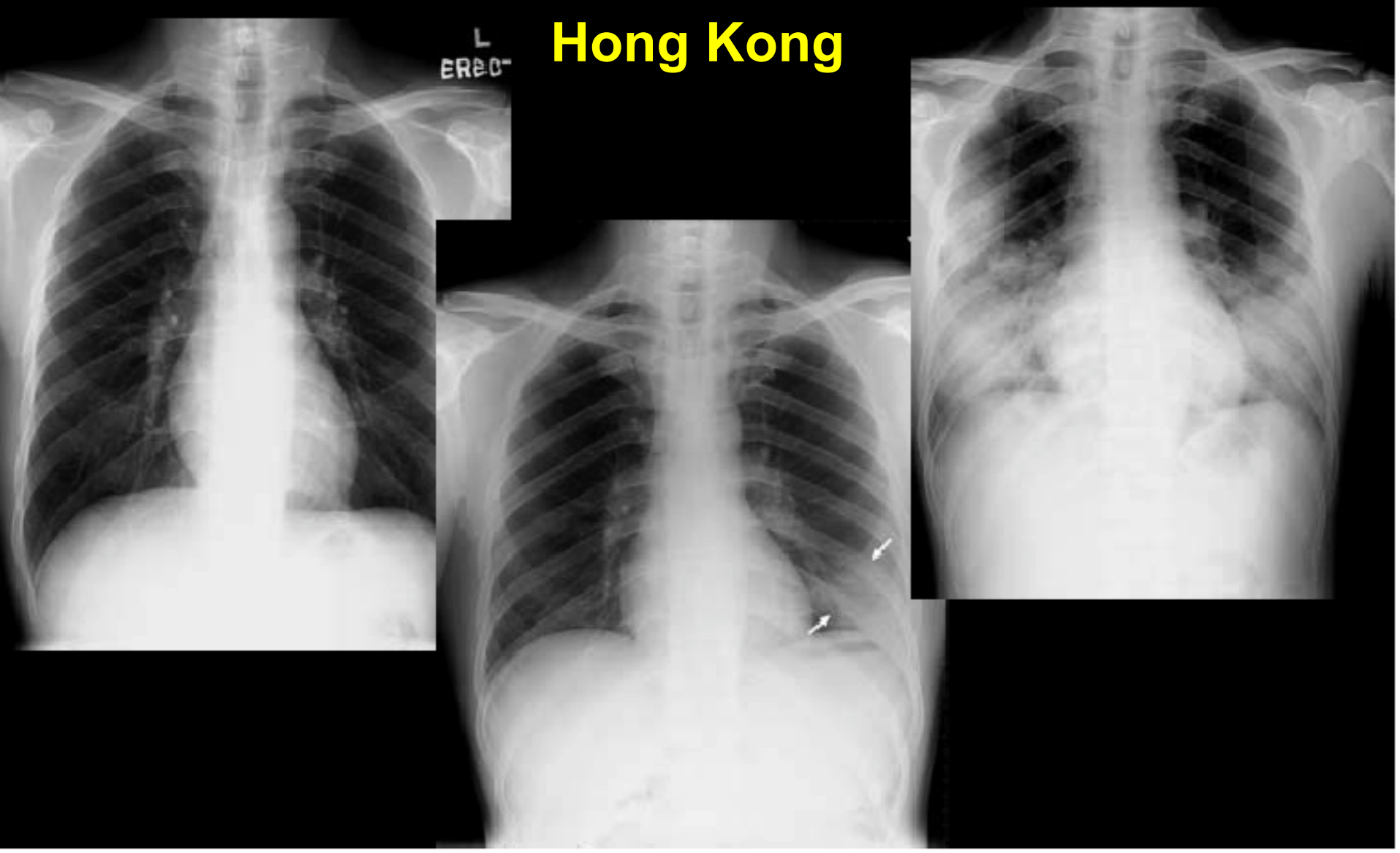
Serum Chemistry

Hong Kong

- Elevated LDH 71%
- Elevated CPK 32%
  - median 126 U/L, range: 29-4644
- Elevated ALT 23%

- Hypokalemia 25%
- Hyponatremia 20%

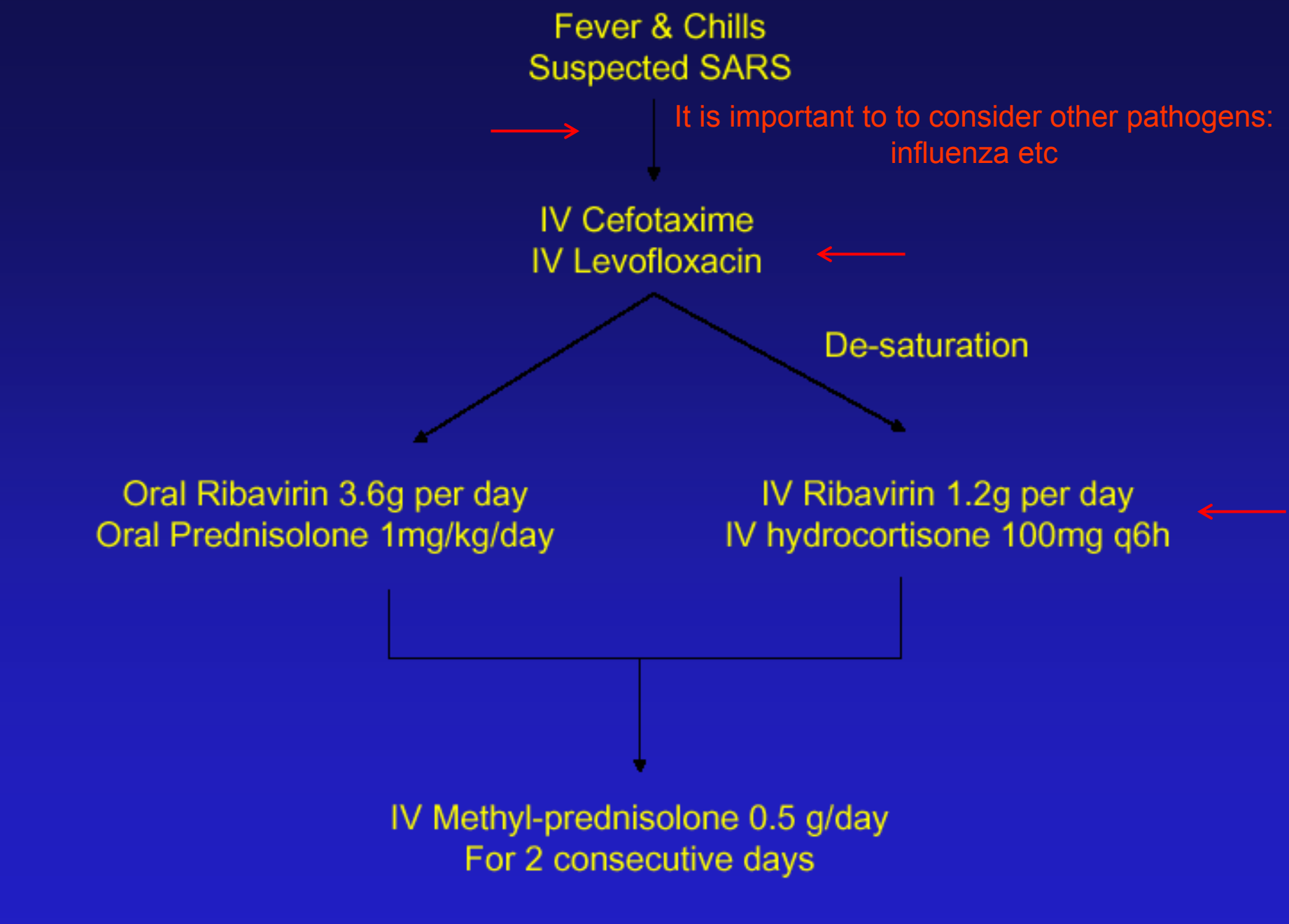
Chest Radiographs



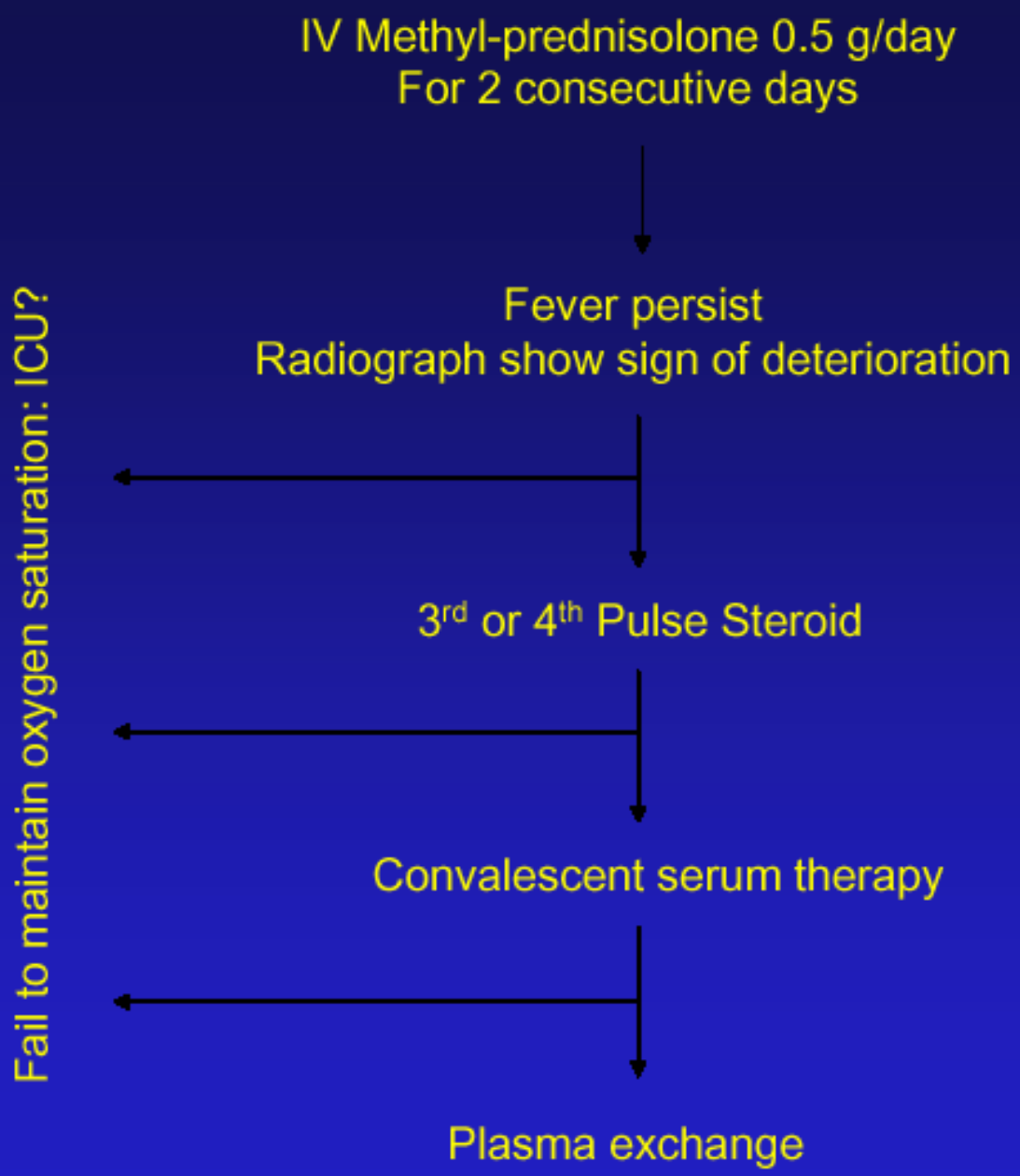
CT Thorax

Hong Kong

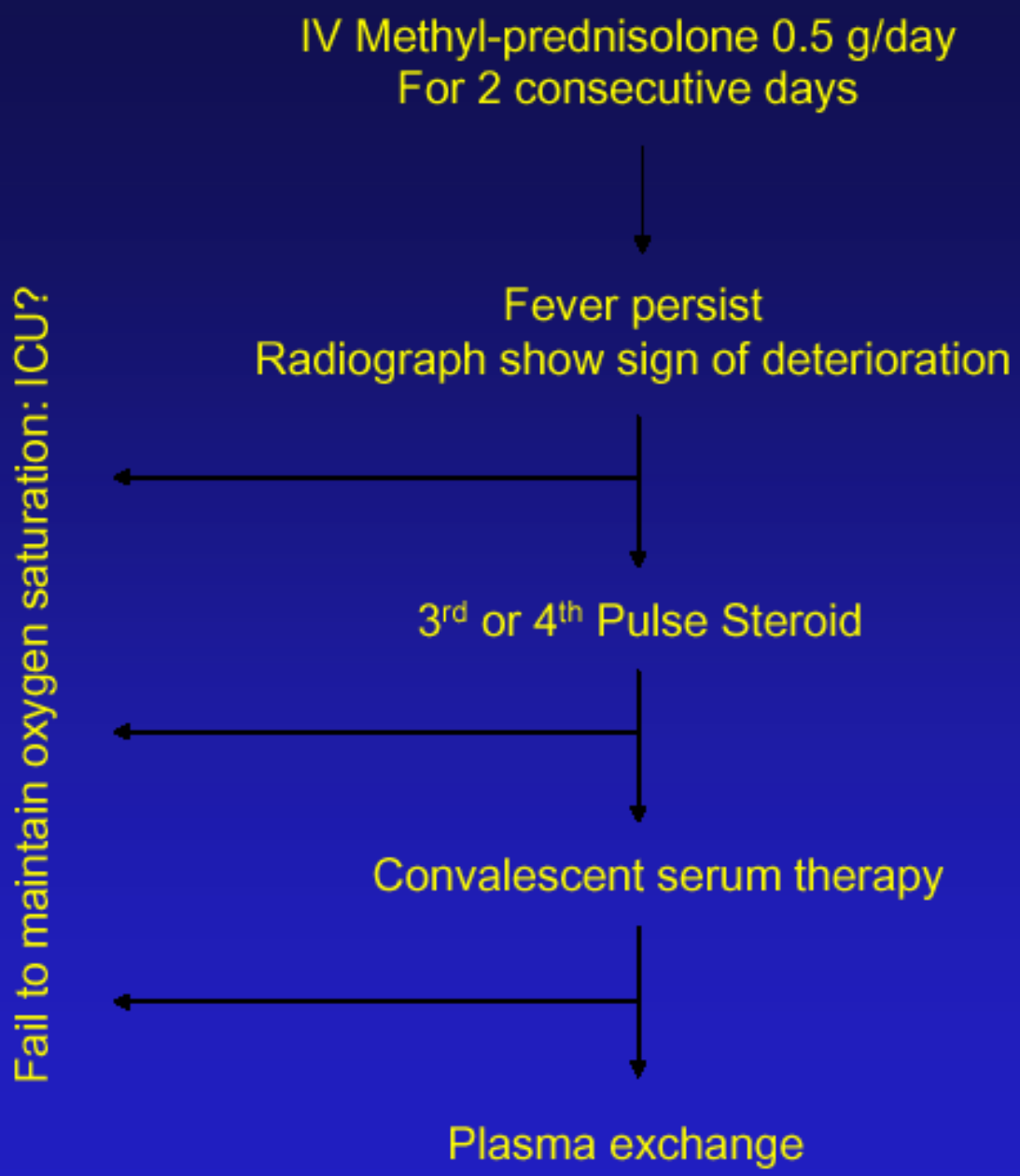
Treatment Protocol – Hong Kong Prince of Wales Hospital 4/1/01



Treatment Protocol – Hong Kong Prince of Wales Hospital 4/1/01



Treatment Protocol – Hong Kong Prince of Wales Hospital 4/1/01

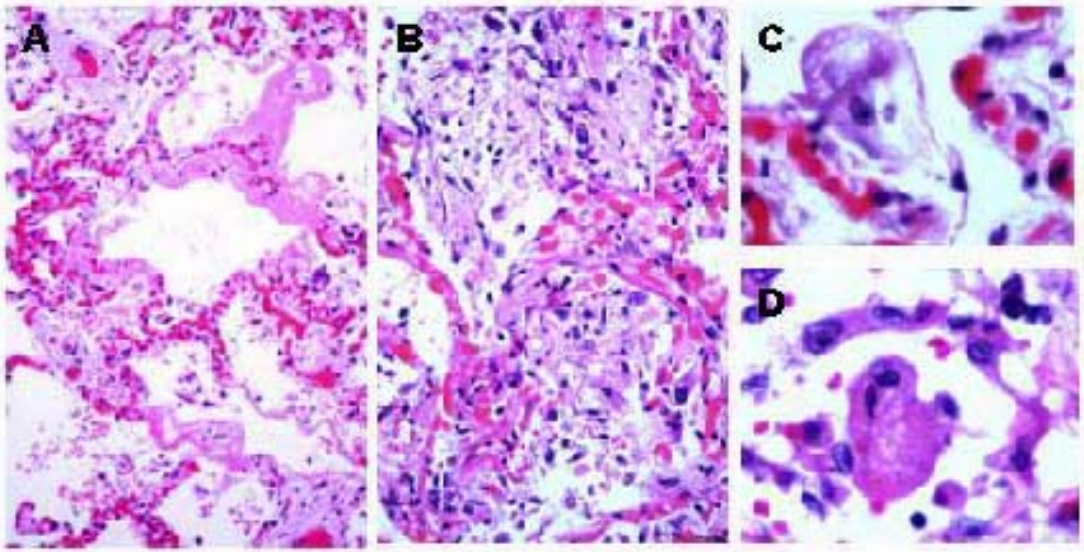


CXR Resolution

Hong Kong

- In 7 days median duration:
  - 82% of patients had 25% resolution of chest shadows
  - 69% of patients had 50% resolution of chest shadows

Postmortem Findings

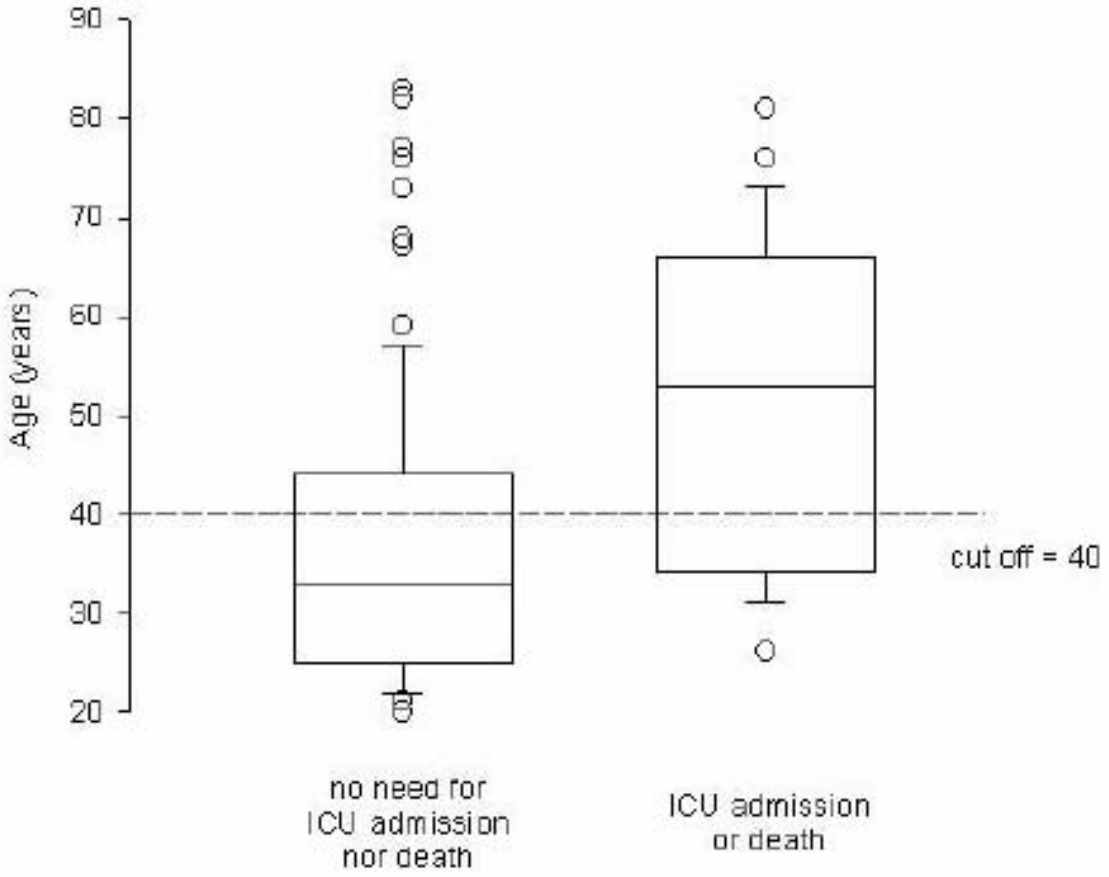


- Early phase of alveolar damage, pulmonary edema, hyaline membrane
- Features suggestive of ARDS.
- Lymphocytic inflammatory infiltrates
- Vacuolated and multi-nucleated pneumocytes
- Viral inclusion

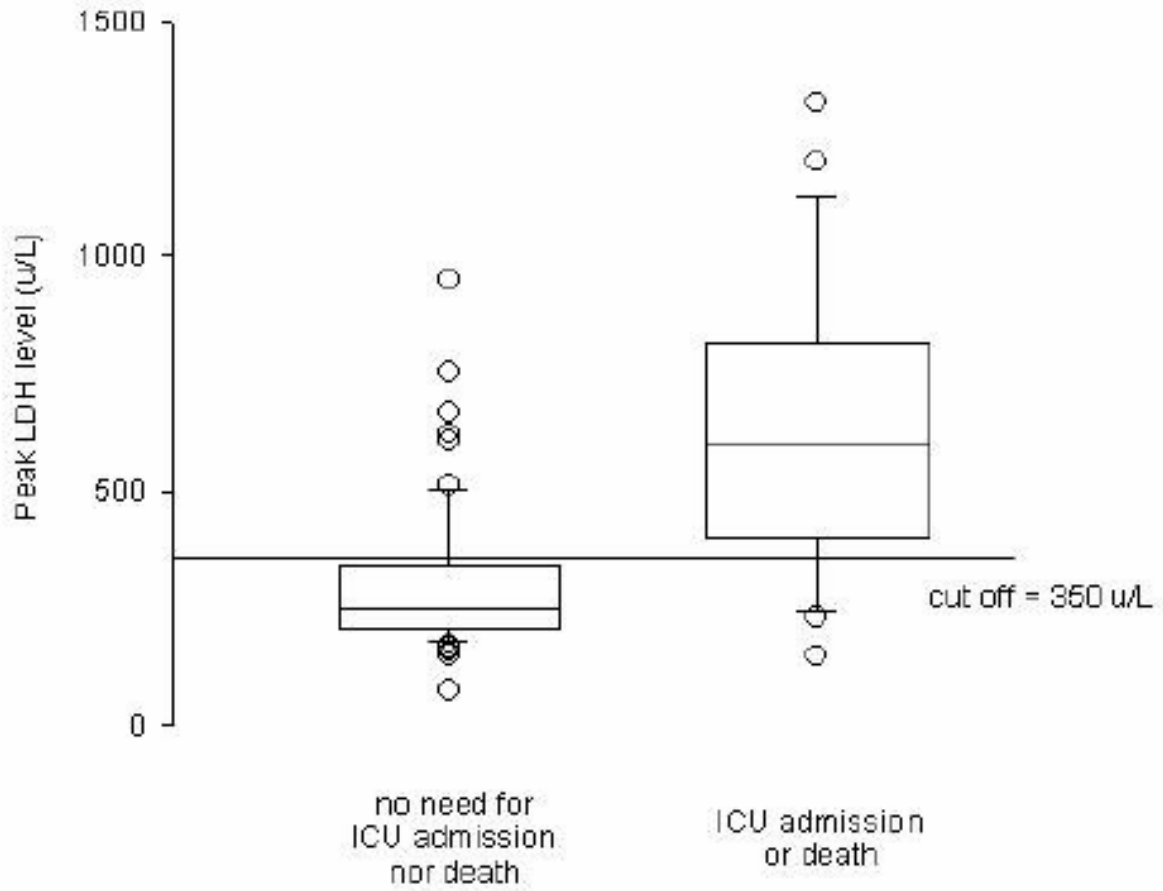
Predictive factor of poor outcome

	No ICU care (mean ± SD)	ICU care or death (mean ± SD)	P value
Age (years)	36.1±14.6	50.2±18.4	0.007
Male sex *	41.9%	66.7%	0.013
Peak D-dimer (ng/ml)	951.0±1197.9	1686.9±2132.3	0.310
Platelet (x 10^9/L)	156.8±61.2	131.7±64.9	0.059
Neutrophil count (x 10^9/L)	3.7±1.9	4.6±2.1	0.021
Lymphocyte count (x 10^9/L)	0.9±0.7	0.8±0.5	0.493
Activated partial thromboplastin time (sec.)	41.0±7.5	43.6±11.7	0.225
Sodium (mmol/L)	136.1±2.7	134.0±4.6	0.022
Urea (mmol/L)	3.8±1.1	7.3±9.6	0.046
Creatinine (μmol/L)	86.1±19.4	135.5±218.0	0.21
Alanine transferase (IU/L)	46.5±81.4	99.4±262.0	0.269
Creatinine kinase on presentation (U/L)	268.5±434.8	609.3±973.2	0.059
Creatinine kinase (peak) (U/L)	352.7±544.0	697.4±971.1	0.043
Lactate dehydrogenase on presentation	287.7±143.3	558.0±258.0	<0.001

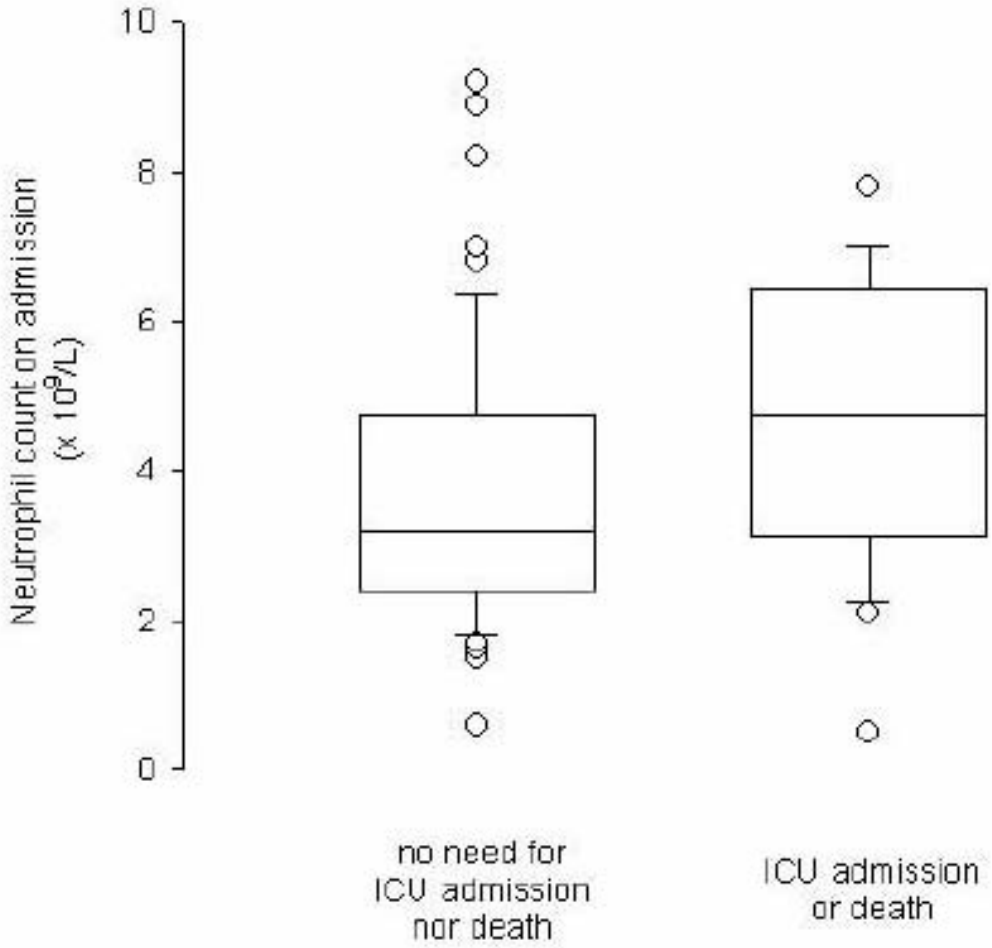
Advanced Age



LDH


1500
1000
500
0
Peak LDH level (u/L)
cut off = 350 u/L
no need for ICU admission nor death
ICU admission or death

Neutrophil count



Side effects of MP

- Superimposed infection 18 (13%)
  - ICU 13 (9.4%)
- Hypokalemia (<3.0): 18 (13%)
- Hyperglycemia (>11.0): 20 (15%)

Lessons Learned

- Early high dose steroid is worthy
- Ribivirin may be beneficial
- Don’t use nebulizer
- Don’t use non-invasive positive pressure ventilation
- Chest physiotherapy may help

Identification of Severe Acute Respiratory Syndrome in Canada

Diabetic, died at home

ER, 2 meters away

Diabetic

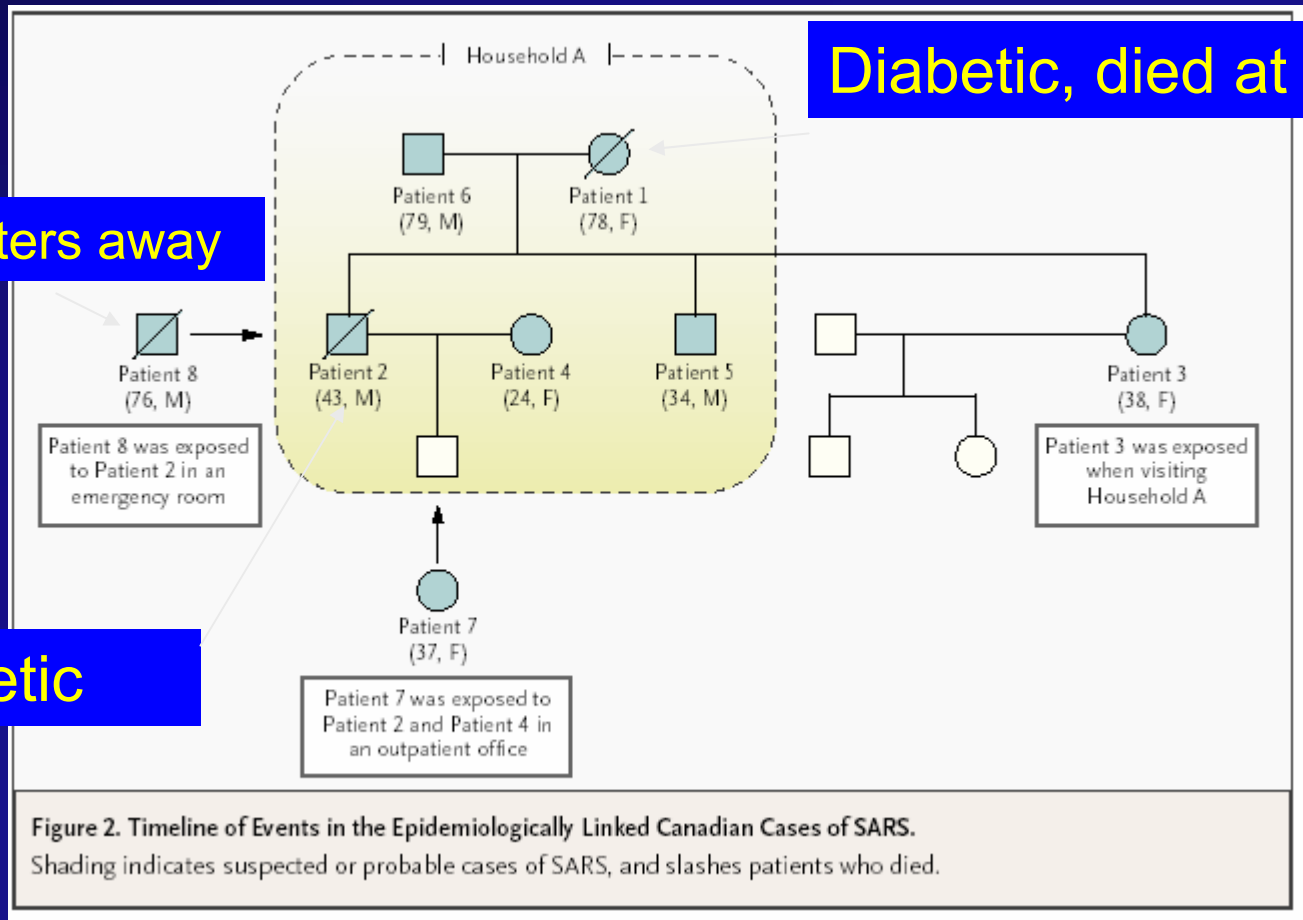


Figure 2. Timeline of Events in the Epidemiologically Linked Canadian Cases of SARS.
Shading indicates suspected or probable cases of SARS, and slashes patients who died.

published at www.nejm.org
on March 31, 2003

Severe Acute Respiratory Syndrome in Canada

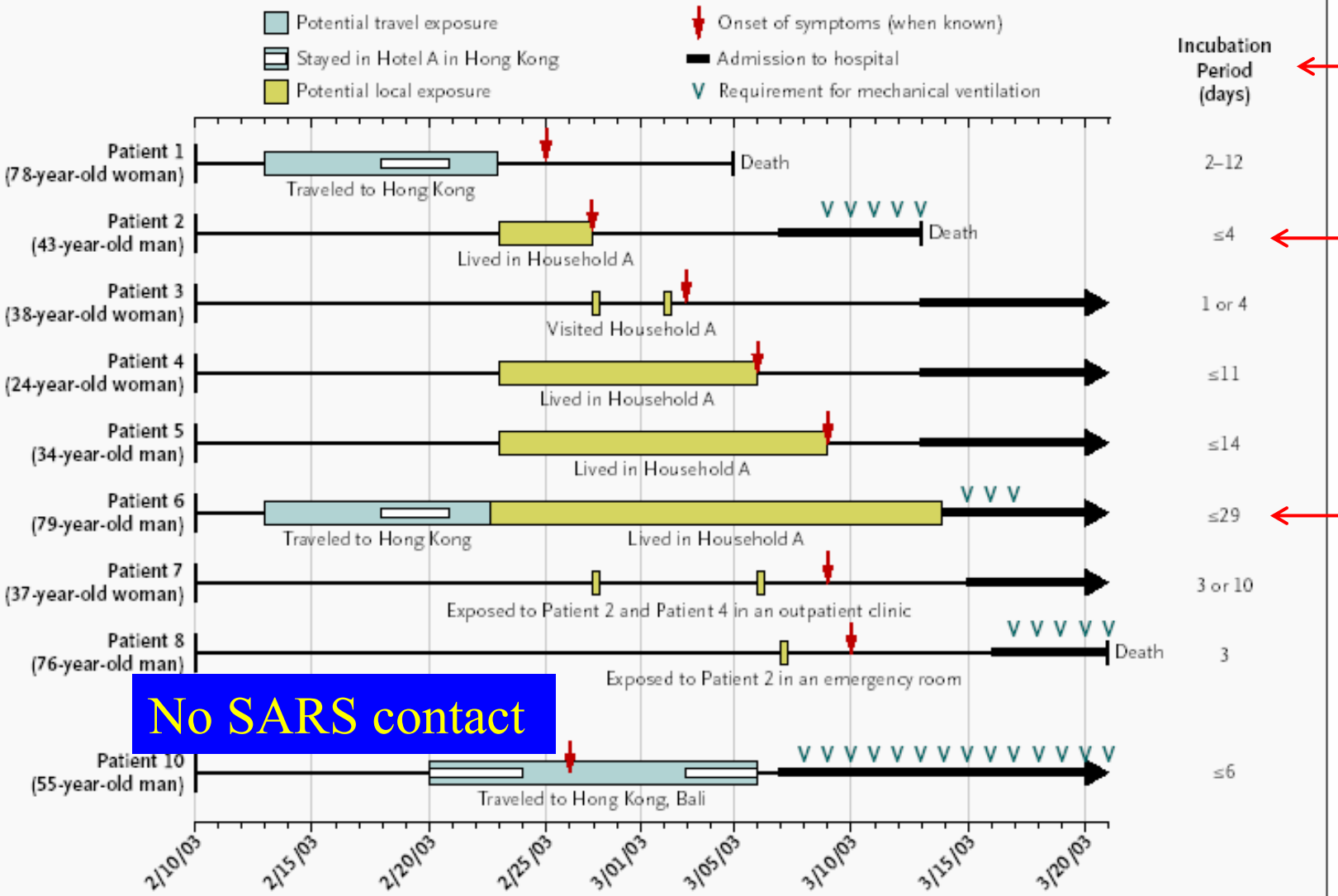


Figure 1. Pedigree of the Epidemiologically Linked Toronto Patients with SARS.

published at www.nejm.org on March 31, 2003

Clinical Features of the Canadian Patients with SARS at Presentation

Symptoms	
Fever	10/10 (100)*
Nonproductive cough	10/10 (100)
Dyspnea	8/10 (80)
Malaise	7/10 (70)
Diarrhea	5/10 (50)
Chest pain	3/10 (30)
Headache	3/10 (30)
Sore throat	3/10 (30)
Myalgias	2/10 (20)
Vomiting	1/10 (10)

Investigations		
Infiltrate on chest radiography	9/9	(100)
Oxygen saturation on room air < 95%	7/9	(78)
Leukopenia (cell count <4× 10^9/liter)	2/9	(22)
Lymphopenia (cell count <1.5× 10^9/liter)	8/9	(89)
Thrombocytopenia (cell count <130× 10^9/liter)	3/9	(33)
Lactate dehydrogenase (above upper limit of normal)	4/5	(80)
Aspartate aminotransferase (>1.5× upper limit of normal)	7/9	(78)
Alanine aminotransferase (>1.5× upper limit of normal)	5/9	(56)
Creatine kinase (above upper limit of normal)	5/9	(56)

published at www.nejm.org
on March 31, 2003

Summary of the 20 cases published at www.nejm.org on March 31, 2003

- Incubation period 1 to 11 days
  - median 5 days
- Fever 100%
- Most patients:
  - Rigor, nonproductive cough, dyspnea, hypoxia, malaise, and headache
  - Lung crackles and dullness on percussion

Summary of the 20 cases published at www.nejm.org on March 31, 2003

- Lymphopenia
- Elevated transaminases
- Hypoxia
- CXR and CT scans
  - Similar to interstitial pneumonia
  - Progressive bilateral air space disease

Summary of the 20 cases published at www.nejm.org on March 31, 2003

- Majority of cases suggest droplet transmission
  - Index cases
  - Family members
  - HCW's
    - *failure to follow infection controls*
- Fourth - and fifth generation of cases
  - Will blur epidemilogical links

Summary of cases

- Increase morbidity and mortality
  - advance age
  - comorbidities e.g. DM
- Ribivirin and prednisone early may be of benefit

Recommended Protocol for Clinical Treatment

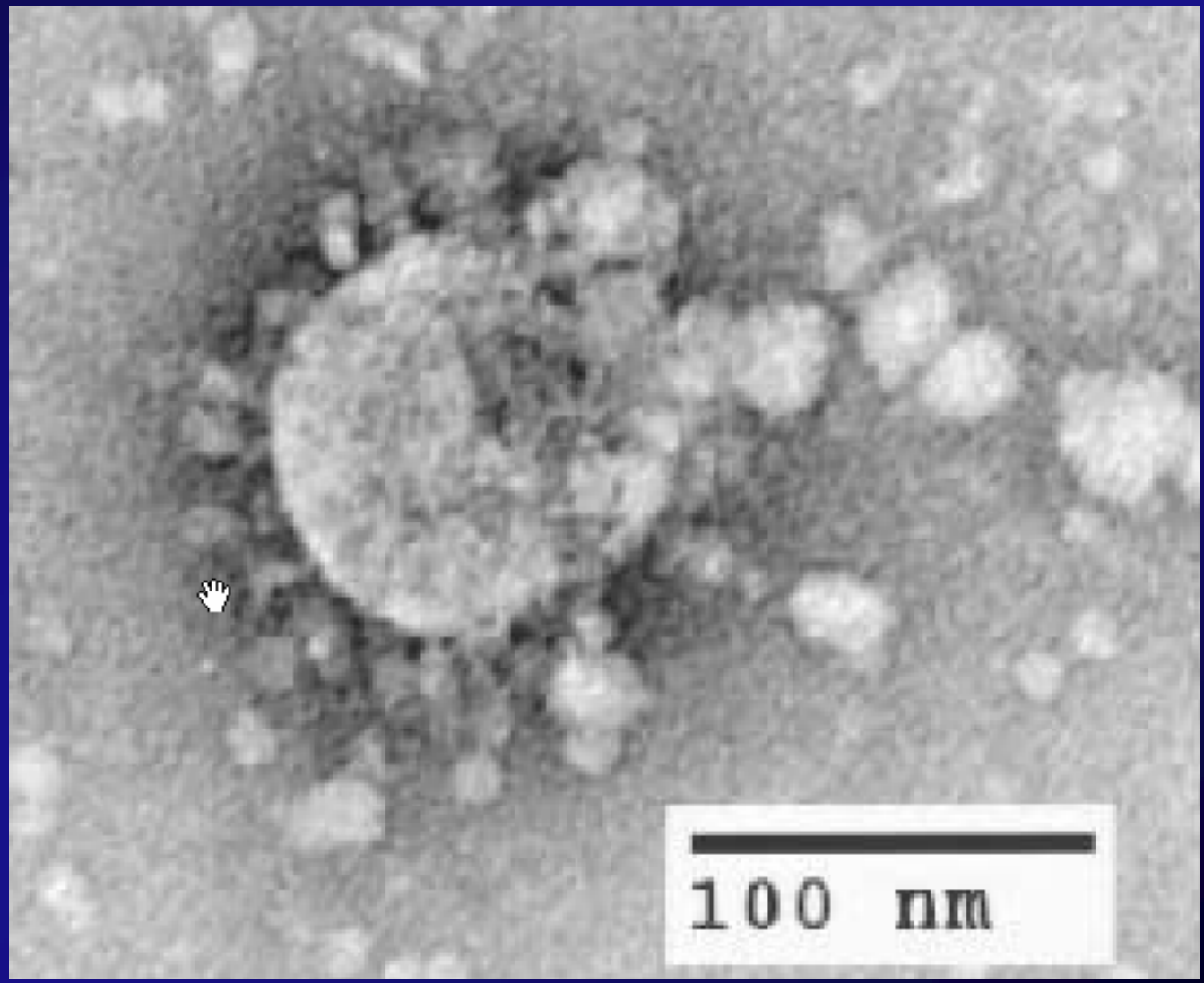
- Community acquired pneumonia protocol
  - 1. R/O influenza
  - 2. Consider atypicals
  - 3. Ribaviran and Prednisone
  - 4. No aerosolized procedures

Prognosis of SARS

- ~ 3 - 4% mortality
- 6% survive but prolong, complicated course
- 90% recover

Coronavirus

Etiology of SARS ?



Laboratory Evidence as of 4/03/2003

Assay	Findings	No. pos. patients*
Culture (Vero E6 cells)	Viral growth	4
EM (cell culture, BAL)	Virus-like particles, Coronavirus	2
PCR (tissue, swabs)	Coronaviral nucleic acid	11
Serology (IFA, EIA)	Antibody	5
Histopathology	DAD (ARDS)	4

*Results not mutually exclusive

CDC

Coronavirus in culture

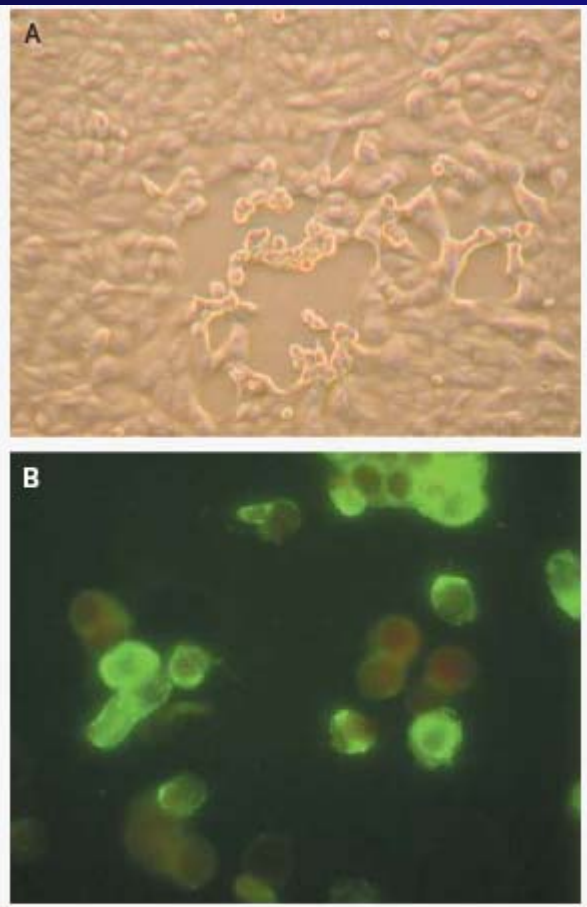


Figure 1. Vero E6 cells Inoculated with Oropharyngeal Specimens from Patients with SARS.

The typical early cytopathic effect seen with coronavirus isolates from patients with SARS is shown in Panel A (×40). Infected Vero cells are shown reacting with the serum of a convalescent patient in an indirect fluorescence antibody assay in Panel B (×400).

This article was published at www.nejm.org on April 10, 2003.

Serological Evidence of Coronavirus

- Found in multiple geographic areas
  - Hong Kong - 9 pts
  - USA - 1
  - Bangkok - 1
  - Singapore - 4
- Seropositivity occurs ~ 11 to 24 days after onset

Multiple Methods Point to Coronavirus

This article was published at www.nejm.org on April 10, 2003.

Table 3. Specimens from Patients with SARS That Were Positive for SARS-associated Coronavirus by One or More Methods.

Patient No.	Exposure	Serologic Results	Specimen	Isolation	PCR
31*	Hong Kong	Positive	Serum	Negative	Not done
39	Hong Kong	Positive	Serum	Negative	Negative
94*	Hong Kong	Positive	Serum	Negative	Negative
220	Hong Kong	Not done	Sputum	Positive	Positive
0	Hong Kong	Positive	Kidney, lung, bronchoalveolar lavage	Positive	Positive
1	Vietnam	Negative	Throat wash	Positive	Positive
3	Vietnam	Negative	Throat wash	Negative	Positive
8	Vietnam	Negative	Throat wash	Negative	Positive
10	Vietnam	Negative	Throat wash	Negative	Positive
13	Vietnam	Negative	Throat wash	Negative	Positive
16	Vietnam	Negative	Throat wash	Negative	Positive
17	Vietnam	Negative	Throat wash	Positive	Positive
20	Vietnam	Negative	Throat wash	Negative	Positive
26	Vietnam	Negative	Throat wash	Negative	Positive
77	Vietnam	Positive	Nasal and throat swab	Positive	Positive
78	Canada	Not done	Lung, bone marrow	Negative	Positive
79	Taiwan	Negative	Sputum	Negative	Positive
80	Hong Kong	Positive	Oropharynx, serum	Negative	Positive

* This was a late specimen, antibody positive at first sample.

Genetic Evidence for Coronavirus

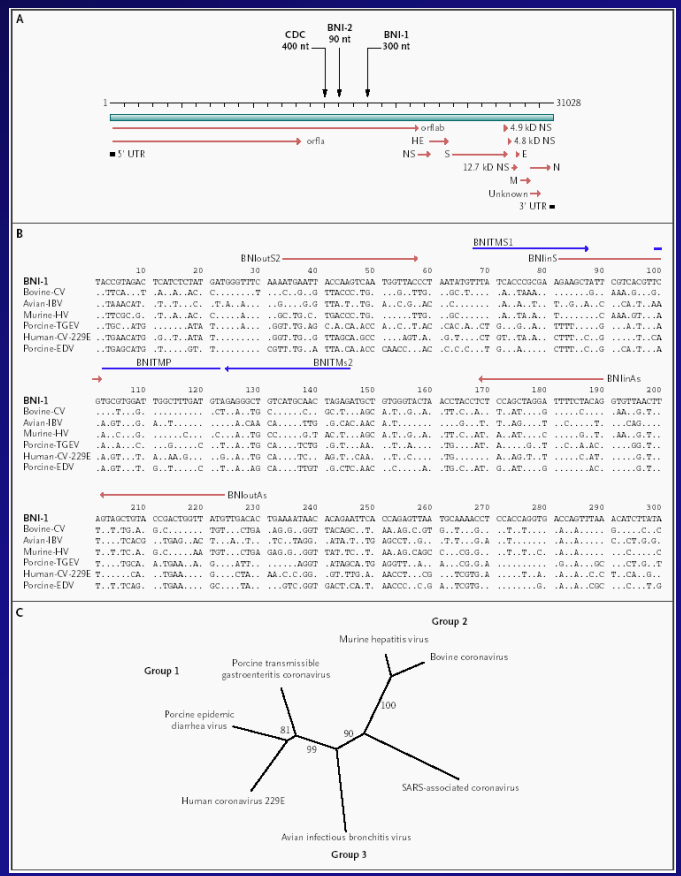


Table 3. Proportion of Patients with a Positive RT-PCR Result for Coronavirus.*

Group	Mean No. of Samples per Patient	Fraction of Patients Testing Positive	
		IN-6/IN-7 and Nested SAR1S/SAR1As	BNIoutS2/BNIoutAs and Nested BNIinS/BNIinAs
Patients with probable SARS †	2.2	5/5	5/5
Patients with suspected SARS‡	1.3	3/13	3/13
Contacts	1.0	0/21	0/21

* RT-PCR denotes reverse-transcriptase polymerase chain reaction.
† Samples were from the lower respiratory tract in 5 patients and nasopharyngeal swabs in 1 patient (all positive); samples were obtained 3 to 13 days after the onset of illness.
‡ Nasopharyngeal samples from 20 patients were used; they were obtained 3 to 12 days after the onset of illness.
§ Samples from 24 contacts were used.

This article was published at www.nejm.org on April 10, 2003.

Coronaviruses

- Single-strand RNA, nonsegmented, enveloped, ~31,000 NTs
- 2 serogroups (229E and OC43) in humans
  - ~1/3 of common colds
  - Reinfections common
- Envelope
  - S - spike protein
  - M - matrix protein
  - HE - hemagglutinin

Coronaviruses

- Survival
  - 229 E
    - 6 days in suspension
    - 3 hrs after drying on surfaces
  - OC43
    - ≤1 hr after drying on surfaces

Coronavirus
Etiology of SARS ?

- Increase confidence in Coronavirus
  - New case definition anticipated
    - To include laboratory test criteria
  - International testing of antiviral compounds
  - Vaccine research underway

SARS Unresolved Issues

- ? Airborne transmission
  - extensive spread within buildings in Asia
- Fomite transmission
  - Coronavirus can survive in the environment for a few hours
  - Coronavirus found in animal stools
- No proven, successful population based strategy prevention

SARS
Optimism for future control

- **Effective coronavirus vaccines in animals**
- **Novel antiviral drugs may be found**
- Infection control measures work

Infection Control

Administrative

- Communication
- Educate
- Policies & procedure
- Enforcement

Personal Protective Measures

- Mask
- Gloves and gowns
- Eye protection
- Hand hygiene

Principles

- Hypertransmitters - some patients
- Protection of patients, staff, visitors
- Prevent spread in the facility and community
- Target all modes of transmission until SARS epidemiology is understood
- Protect facilities so routine care is not impaired

Triage for SARS in Ambulatory Care

- Targeted screening
- Currently:
  - Travel history
  - Contact with a person with SARS
  - Air travel to a country with SARS
  - Fever and or respiratory symptoms

www.cdc.gov/ncidod/sars/triage_interim_guidance.pdf

Triage for SARS in Ambulatory Care

- Evaluate in a separate assessment area
- If SARS suspected:
  - Patient wears a surgical mask
  - HCW applies Airborne and Contact Precautions
    - N95 if available; at least a surgical mask
    - Gloves
    - Gown
    - Eye protection
    - Negative pressure if available

Respiratory Protection

- Patient
  - Cover coughs with tissue or hand
  - Surgical mask
  - Hand hygiene
- Healthcare Workers
  - N95
  - PAPR
  - Surgical mask if respirator not available

Engineering measures

- Control of ventilation
- Control of traffic
- Security

Aerosolizing Procedures for SARS

- **Evaluate patients for SARS before:**
  - Aerosolized medication treatments
  - Sputum induction
  - Bronchoscopy
  - Airway suctioning
  - Endotracheal intubation

- **Perform only if medically necessary**
- **Use Airborne Precautions as per TB**

www.cdc.gov/ncidod/sars/pdf/aerosolinfectioncontrol-sars.pdf

Visitor Restrictions

- Symptomatic close contacts of SAR patients should not enter facility.
- Screening.
- Educate visitors about precautions if visiting a SARS patient.

Post-mortem

- Standard Precautions
  - Gown
  - N95, N100, or PAPR (preferred for aerosolizing procedures)
- Autopsy
  - Minimum 12 ACH and negative pressure
  - Prevent percutaneous injury
  - Dispose of PPE carefully

www.cdc.gov/ncidod/sars/pdf/sarsautopsy.pdf

Patients with suspected SARS and Household Contacts

- Limit interactions outside the home until 10 days after resolution of symptoms
- Hand hygiene
- Gloves
- Patient covers coughs with tissue or mask
- Do not share utensils, towels, bedding
- Clean surfaces with disinfectant
- Household contacts do not limit activity outside the home if asymptomatic

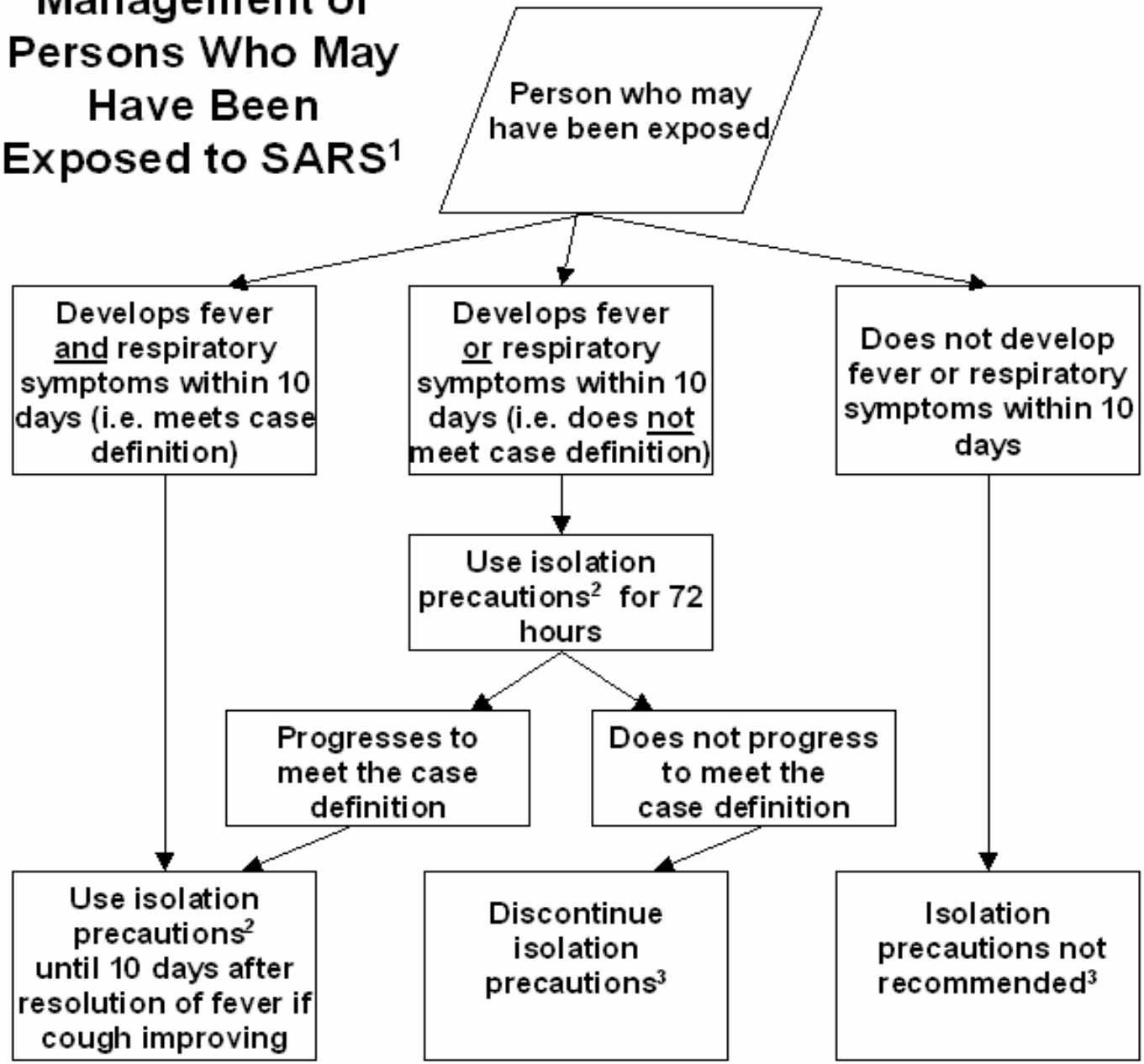
www.cdc.gov/ncidod/sars/pdf/ic-closecontacts-sars.pdf

Exposure Management

Definitions

- Exposure:Travel from areas with documented or suspected community transmission of SARS
- Close Contact
  - having cared for
  - having lived with
  - having direct contact with respiratory secretions and/or body fluids

Management of Persons Who May Have Been Exposed to SARS[1]



www.cdc.gov/ncidod/sars/pdf/exposuremanagement-sars.pdf

Exposure Management in Healthcare

- Transmission associated with unprotected exposure
- Exclude from duty if symptomatic within 10 days of exposure to SARS. Continue until 10 days after resolution of symptoms.
- Screen exposed daily for fever and respiratory symptoms.
- Facilities with SARS patients:
  - educate workers about symptoms
  - passive surveillance

www.cdc.gov/ncidod/sars/pdf/exposureguidance.pdf

School Children Exposed to SARS

- No symptoms-do not exclude from school but monitor symptoms
- Fever or respiratory symptoms within 10 days of exposure
  - Stay home; if no progression to SARS, then return to school
  - If progresses to SARS, precautions continued until 10 days after resolution
  - Alternative housing for students in dorms, etc.

www.cdc.gov/ncidod/sars/pdf/exposurestudents.pdf

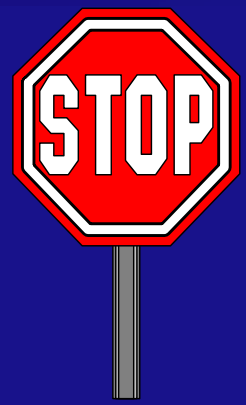
Advice for Travelers

- Know about SARS in the travel area
- Do not go to China, Hong Kong, Singapore or Hanoi unless necessary.
- No advisories about Canada.
- Current immunizations.
- Hand hygiene; bring alcohol hand rubs
- Seek medical attention if ill

www.cdc.gov/ncidod/sars/pdf/travel_advice.pdf

SARS Infection Control at Altru Phase 1

- Identify and rapidly isolate initial patients
  - Signs at entry: passive screening
  - First contacts screen for travel and SARS exposure
  - EOD: active screening
  - SARS Call Center
  - Use existing negative pressure rooms
  - Education



SARS ALERT

Severe Acute Respiratory Syndrome

PLEASE PUT ON A MASK IF:

You have traveled to any of these areas in the last 3 weeks:

- **Asia**, including:
  China, Hong Kong, Hanoi, Vietnam, or Singapore
- **Toronto**, Canada

AND

You are ill with:

- **FEVER** higher than 100.4° F
- Respiratory illness
  - **COUGH**
  - Shortness of breath
  - Difficulty breathing
  - Respiratory distress

OR

Have had close contact with a person known or suspected to have SARS.

Altru Health System

APRIL 7. 2003

Summary

- Use epidemiology
- Passive and active screening
- Use standard, airborne, and contact precautions